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REVISED CLAIMS

1. A method of expanding and selecting disease associated, antigen activated continuous T-cells comprising

(a) obtaining a tissue sample from a mammal including a human being, the sample comprising disease associated, antigen activated T-cells and disease associated antigen or antigens, or

obtaining T-cells, comprising disease associated, antigen activated T-cells, and antigen-presenting cell from said mammal and mixing said cells with a disease associated antigen or antigens, and

(b) culturing said tissue sample or said mixture of cells and antigen(s) in the presence of at least two factors which promote T-cell growth and optionally one or more additional compounds.

2. A method according to claim 1, wherein the factors which promote T-cell growth are selected from the group consisting of cytokines which promote T-cell growth.

3. A method according to claim 2, wherein the cytokines are selected from the group consisting of IL-2, IL-4, IL-7, IL-9, IL-10, IL-15, IL-16 and functionally similar cytokines.

4. A method according to ~~any one of claims 1-3~~ claim 1, wherein a combination of IL-2 and/or IL-15 and IL-4 and/or IL-7 and/or IL-9 is used.

5. A method according to ~~any of claims 1-4~~ claim 1, wherein a combination of IL-2 and IL-4 is used.

6. A method according to ~~any one of claims 1-5~~ claim 1, wherein each of the cytokines is used in a concentration of at least 1 nM, preferably more than 2.5 nM, more preferably more than 10 nM.

7. A method according to ~~any one of claims 1-6~~ claim 1, wherein the tissue sample is selected from a biopsy, from sputum, swaps, gastric lavage, bronchial lavage, intestinal lavage, or body fluids such as spinal, pleural, pericardial, synovial, blood and bone marrow.

8. A method according to ~~any one of claims 1-7~~ claim 1, wherein the disease associated, antigen activated T-cells are CD4+, CD8+ or CD4-/CD8- T-cells.

9. A method according to ~~any one of claims 1-8~~ claim 1, wherein the disease associated, antigen activated T-cells are selected from the group consisting of inflammatory, cytotoxic and regulatory T-cells.

10. A method according to ~~any one of claims 1-9~~ claim 1, wherein the disease associated, antigen activated T-cells are associated with a disease of inflammatory, auto-immune, allergic, neoplastic or transplantation-related origin, or combinations thereof.

11. A method according to claim 10, wherein the disease of inflammatory or allergic origin is a chronic inflammatory disease, or a chronic allergic disease.

12. A method according to ~~any one of claims 1-11~~ claim 1, wherein the ~~disease~~ is an chronic inflammatory bowel disease, such as Crohn's ~~disease~~ or ulcerative colitis, multiple sclerosis, type I ~~diabetes~~, rheumatoid arthritis, psoriasis, atopic dermatitis, ~~asthma~~, malignant melanoma, renal carcinoma, breast cancer, lung ~~cancer~~, cancer of the uterus, prostatic cancer, cutaneous lymphoma, hepatic carcinoma, rejection-related disease, or Graft-versus-host-related disease.

13. A method according to ~~any one of claims 1-12~~ claim 1, wherein the additional compound is selected from the group consisting of compounds which directly or indirectly interfere with T-cell growth.

14. A method according to claim 13, wherein the compound enhances or inhibits the growth of a certain subgroup of T-cells, such as inflammatory, regulatory or cytotoxic T-cells.

15. A method according to claim 13 ~~or claim 14~~, wherein the compound is selected from the group consisting of cyclosporin, GM-CSF, Prednisone, Tacrolimus, FK506, IL-10, anti-IL-10, TNFα antibody, IL-12, anti-IL-12, IL-7, anti-IL-7, IL-9, anti-IL-9, IL-16, caspase inhibitors, and functionally similar compounds.

16. A method according to ~~any one of claims 1-15~~ claim 1 further comprising a selection procedure.

17. A method according to ~~any one of the claims 1-16~~ claim 1, wherein disease associated, antigen activated inflammatory T-cells are expanded and selected.

18. A method according to claim 17, wherein the inflammatory T-cells are cells having a CD4+ phenotype and a type 1 cytokine profile.

19. A method according to claim 18, wherein the inflammatory T-cells are cells contributing in a type 1 inflammatory infiltrate producing IFNγ and TNFα.

20. A method according to claim 18 ~~or claim 19~~, wherein the one or more additional compounds is selected from cyclosporine, Prednisone, Tacrolimus, FK506, GM-CSF, IL-12, IL-16, anti-IL-10, anti-TNFα, and functionally similar compounds.

21. A method according to claim 17, wherein the inflammatory T-cells are cells having a CD4+ phenotype and a type 2 cytokine profile.

22. A method according to claim 21, wherein the inflammatory T-cells are cells contributing in a type 2 inflammatory infiltrate producing IL-4 or IL-5.

23. A method according to claim 21 ~~or claim 22~~, wherein the one or more additional compound is selected from cyclosporine, Prednisone, Tacrolimus, FK506, GM-CSF, IL-16, anti-IL-12, and functionally similar compounds.

24. A ~~method~~ according to ~~any one of claims 17-23~~ claim 17, wherein the disease is mediated or partially mediated by type 1 or type 2 inflammatory T-cells, such as chronic inflammatory bowel diseases, for example Crohn's disease and ulcerative colitis, multiple sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, and asthma.

25. A method according to ~~any one of the claims 1-16~~ claim 1, wherein disease associated, antigen activated regulatory T-cells are expanded and selected.

26. A method according to claim 25, wherein the regulatory T-cells are cells having a CD4+ phenotype and a type 1 cytokine profile regulating a type 2 inflammatory disease.

27. A method according to ~~claim~~ 26, wherein the regulatory T-cells are cells producing INFγ.

28. A method according to claim 26 ~~or claim 27~~, wherein the one or more additional compounds is selected from IL-12 and functionally similar compounds.

29. A method according to ~~any one of claims 25-28~~ claim 25, wherein the disease is mediated or partly mediated by type 2 inflammatory T-cells such as asthma or atopic dermatitis.

30. A method according to claim 25, wherein the regulatory T-cells are cells having a CD4+ phenotype and a type 2 cytokine profile regulating a type 1 inflammatory disease.

31. A method according to claim 30, wherein the regulatory T-cells are cells producing IL-10 and/or IL-4.

32. A method according to claim 30 ~~or 31~~, wherein the one or more additional compounds is selected from anti-IL-12, IL-10, GM-CSF, IL-16, and functionally similar compounds.

33. A method according to ~~any of claims 30-32~~ claim 30, wherein the disease is mediated or partially mediated by type 1 inflammatory T-cells, such as chronic inflammatory bowel

diseases, for example Crohn's disease and ulcerative colitis, multiple sclerosis, type I diabetes, rheumatoid arthritis, and psoriasis.

34. A method according to ~~any one of the claims 1-16~~ claim 1, wherein disease associated, antigen activated cytotoxic T-cells are expanded and selected.

35. A method according to claim 34, wherein the cytotoxic T-cells are cells having a CD8+ phenotype.

36. A method according to claim 34 ~~or claim 35~~, wherein the cytotoxic T-cells are tumour infiltrating lymphocytes (TIL) or cells having similar properties.

37. A method according to ~~any of claims 34-35~~ claim 34, wherein the one or more additional compounds is selected from GM-CSF, caspase inhibitors such as Z-VAD, α-CD95, IL-10, IL-12, IL-16, and functionally similar compounds.

38. A method according to ~~any of claims 34-38~~ claim 34, wherein the disease is of neoplastic origin.

39. A method according to ~~any one of claims 34-38~~ claim 34 wherein the disease is malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, prostatic cancer, hepatic carcinoma, or cutaneous lymphoma.

40. A disease associated, antigen activated continuous T-cell line obtainable by a method according to ~~any of claims 1-39~~ claim 1.

41. A T-cell line according to claim 40, wherein the T-cells are inflammatory T-cells.

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42. A T-cell line according to claim 40, wherein the T-cells are regulatory T-cells.

43. A T-cell line according to ~~claim~~ 40, wherein the T-cells are cytotoxic T-cells.

44. A vaccine comprising activated disease associated, antigen activated inflammatory T-cells prepared according to the method of ~~any one of claims 1-24~~ claim 1, or a continuous disease associated, antigen activated T-cell line according to claim 41.

45. A vaccine according to claim 44, wherein T-cells are re-activated in the presence of one or more antigens.

46. A vaccine according to claim 45, wherein the antigen or antigens is disease associated antigen(s), alloantigen(s) or super-antigen(s).

47. A vaccine according to claim 46, wherein the superantigens are selected from SEA, SEB, SEC, SED, SEE, TSST, Streptococcus pyogenes enterotoxin A, B and C, and Mycoplasma arthritidis antigen.

48. A vaccine according to ~~any one of claims 44-47~~ claim 44, wherein the T-cells have been attenuated.

49. Use of a continuous disease associated, antigen activated T-cell line according to ~~any of claims 40-43~~ claim 40, or disease associated, antigen activated T-cells prepared according to any of the claims 1-39 in the preparation of a medicament for the treatment of a T-cell associated disease.

50. Use according to claim 49, wherein the disease is a disease of inflammatory, auto-immune, allergic,

neoplastic or transplantation-related origin, or combinations thereof.

51. Use according to claim 50, wherein the disease is an inflammatory bowel disease, such as Crohn's disease and Ulcerative colitis, multiple sclerosis, type I diabetes, rheumatoid arthritis, psoriasis, atopic dermatitis, asthma, malignant melanoma, renal carcinoma, breast cancer, lung cancer, cancer of the uterus, prostatic cancer, cutaneous lymphoma, asthma, rejection-related disease, or Graft-versus-host-related disease.

52. A method for the treatment, alleviation or prevention of a disease associated with an activation of T-cells in a subject comprising administering a continuous disease associated, antigen activated T-cell line according to ~~any of claims 40-43~~ claim 40, disease associated, antigen activated T-cells as produced according to any of claims 1-39, or a vaccine according to claims 44-48 to said subject.

53. A method according to claim 52, wherein the T-cells are expanded from a tissue sample collected from the patient to be treated.

54. A method according to claim 52, wherein the T-cells are expanded from a tissue ~~sample~~ collected from a patient different to the patient to be treated.

55. A method according to ~~claim~~ 54, further comprising determining the HLA restriction in the T-cells and in the patient to be treated.